

## FXR MODULATORS

### ABSTRACT OF THE DISCLOSURE

5           The present invention provides compounds, pharmaceutical compositions  
and methods that are useful in modulating the farnesoid X receptor (FXR). As FXR is  
involved in negatively controlling the expression level of cholesterol 7 $\alpha$ -hydroxylase  
(*cyp7a*), the rate-limiting enzyme involved in the oxidative metabolism of cholesterol into  
10   bile acids, the compounds described herein find utility in treating diseases associated with  
abnormally high or low cholesterol levels. In certain aspects, the FXR modulators (*e.g.*,  
antagonists) described herein block the negative feed-back downregulation of *cyp7a*  
expression produced by certain cholic acids, the endogenous ligands for FXR. Moreover,  
as FXR forms heterodimers with the retinoid X receptor (RXR) in some cell types,  
modulation of the level of FXR activity in cells has a wide range of effects on a variety of  
15   biological processes which are mediated by RXR or other RXR-interacting proteins such  
as PPAR $\gamma$  and PPAR $\alpha$ . Thus, compounds described herein are useful in treating other  
biological activities such as obesity, diabetes, lipid associated disorders, cancer,  
inflammatory disorders, disorders involving a disrupted or dysfunctional epidermal  
barrier, and various other metabolic disorders.

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